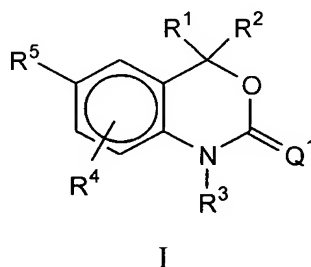


What is Claimed:

1. A method of treating acne and/or hirsutism comprising the step of delivering to a mammal in need thereof a composition comprising a compound of formula I, or a tautomer thereof, and a physiologically compatible carrier, wherein formula I is:



wherein:

$R^1$  and  $R^2$  are independent substituents selected from the group consisting of H,  $C_1$  to  $C_6$  alkyl, substituted  $C_1$  to  $C_6$  alkyl,  $C_2$  to  $C_6$  alkenyl, substituted  $C_2$  to  $C_6$  alkenyl,  $C_2$  to  $C_6$  alkynyl, substituted  $C_2$  to  $C_6$  alkynyl,  $C_3$  to  $C_8$  cycloalkyl, substituted  $C_3$  to  $C_8$  cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms,  $COR^A$ , and  $NR^B COR^A$ ;

or  $R^1$  and  $R^2$  are fused to form a ring selected from the group consisting of a), b) and c), wherein said ring is optionally substituted by from 1 to 3 substituents selected from the group consisting of H and  $C_1$  to  $C_3$  alkyl;

a) a carbon-based 3 to 8 membered saturated spirocyclic ring;

b) a carbon-based 3 to 8 membered spirocyclic ring having one or more carbon-carbon double bonds; and

c) a 3 to 8 membered spirocyclic ring having in its backbone one to three heteroatoms selected from the group consisting of O, S and N;

$R^A$  is selected from the group consisting of H,  $C_1$  to  $C_3$  alkyl, substituted  $C_1$  to  $C_3$  alkyl, aryl, substituted aryl,  $C_1$  to  $C_3$  alkoxy, substituted  $C_1$  to  $C_3$  alkoxy, amino,  $C_1$  to  $C_3$  aminoalkyl, and substituted  $C_1$  to  $C_3$  aminoalkyl;

$R^B$  is selected from the group consisting of H,  $C_1$  to  $C_3$  alkyl, and substituted  $C_1$  to  $C_3$  alkyl;

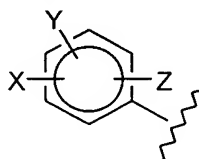
$R^3$  is selected from the group consisting of H, OH,  $NH_2$ ,  $C_1$  to  $C_6$  alkyl, substituted  $C_1$  to  $C_6$  alkyl,  $C_3$  to  $C_6$  alkenyl, substituted  $C_3$  to  $C_6$  alkenyl, alkynyl, substituted alkynyl, and  $COR^C$ ;

$R^C$  is selected from the group consisting of H,  $C_1$  to  $C_4$  alkyl, substituted  $C_1$  to  $C_4$  alkyl, aryl, substituted aryl,  $C_1$  to  $C_4$  alkoxy, substituted  $C_1$  to  $C_4$  alkoxy,  $C_1$  to  $C_4$  aminoalkyl, and substituted  $C_1$  to  $C_4$  aminoalkyl;

$R^4$  is selected from the group consisting of H, halogen, CN,  $NO_2$ ,  $C_1$  to  $C_6$  alkyl, substituted  $C_1$  to  $C_6$  alkyl,  $C_1$  to  $C_6$  alkoxy, substituted  $C_1$  to  $C_6$  alkoxy,  $C_1$  to  $C_6$  aminoalkyl, and substituted  $C_1$  to  $C_6$  aminoalkyl;

$R^5$  is selected from the group consisting of (i) and (ii):

(i) a substituted benzene ring having the structure:



X is selected from the group consisting of halogen, CN,  $C_1$  to  $C_3$  alkyl, substituted  $C_1$  to  $C_3$  alkyl,  $C_1$  to  $C_3$  alkoxy, substituted  $C_1$  to  $C_3$  alkoxy,  $C_1$  to  $C_3$  thioalkyl, substituted  $C_1$  to  $C_3$  thioalkyl,  $C_1$  to  $C_3$  aminoalkyl, substituted  $C_1$  to  $C_3$  aminoalkyl,  $NO_2$ ,  $C_1$  to  $C_3$  perfluoroalkyl, substituted  $C_1$  to  $C_3$  perfluoroalkyl, 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms,  $COR^D$ ,  $OCOR^D$ , and  $NR^E COR^D$ ;

$R^D$  is selected from the group consisting of H,  $C_1$  to  $C_3$  alkyl, substituted  $C_1$  to  $C_3$  alkyl, aryl, substituted aryl,  $C_1$  to  $C_3$  alkoxy, substituted  $C_1$  to  $C_3$  alkoxy,  $C_1$  to  $C_3$  aminoalkyl, and substituted  $C_1$  to  $C_3$  aminoalkyl;

$R^E$  is selected from the group consisting of H,  $C_1$  to  $C_3$  alkyl, and substituted  $C_1$  to  $C_3$  alkyl;

Y and Z are independent substituents selected from the group consisting of H, halogen, CN, NO<sub>2</sub>, C<sub>1</sub> to C<sub>3</sub> alkoxy, substituted C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>4</sub> alkyl, substituted C<sub>1</sub> to C<sub>4</sub> alkyl, C<sub>1</sub> to C<sub>3</sub> thioalkyl, and substituted C<sub>1</sub> to C<sub>3</sub> thioalkyl; and

b) a five or six membered carbon-based heterocyclic ring having in its backbone 1, 2, or 3 heteroatoms selected from the group consisting of O, S, SO, SO<sub>2</sub>, and NR<sup>6</sup> and having one or two independent substituents selected from the group consisting of H, halogen, CN, NO<sub>2</sub>, C<sub>1</sub> to C<sub>4</sub> alkyl, substituted C<sub>1</sub> to C<sub>4</sub> alkyl, C<sub>1</sub> to C<sub>3</sub> alkoxy, substituted C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>3</sub> aminoalkyl, substituted C<sub>1</sub> to C<sub>3</sub> aminoalkyl, C<sub>1</sub> to C<sub>3</sub> perfluoroalkyl, substituted C<sub>1</sub> to C<sub>3</sub> perfluoroalkyl, 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, C<sub>1</sub> to C<sub>3</sub> thioalkyl, substituted C<sub>1</sub> to C<sub>3</sub> thioalkyl, COR<sup>F</sup>, and NR<sup>G</sup>COR<sup>F</sup>;

R<sup>F</sup> is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, substituted C<sub>1</sub> to C<sub>3</sub> alkyl, aryl, substituted aryl, C<sub>1</sub> to C<sub>3</sub> alkoxy, substituted C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>3</sub> aminoalkyl, and substituted C<sub>1</sub> to C<sub>3</sub> aminoalkyl;

R<sup>G</sup> is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, and substituted C<sub>1</sub> to C<sub>3</sub> alkyl;

R<sup>6</sup> is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, and C<sub>1</sub> to C<sub>4</sub> CO<sub>2</sub>alkyl;

Q<sup>1</sup> is selected from the group consisting of S, NR<sup>7</sup>, and CR<sup>8</sup>R<sup>9</sup>;

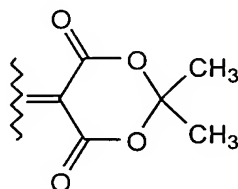
R<sup>7</sup> is selected from the group consisting of CN, C<sub>1</sub> to C<sub>6</sub> alkyl, substituted C<sub>1</sub> to C<sub>6</sub> alkyl, C<sub>3</sub> to C<sub>8</sub> cycloalkyl, substituted C<sub>3</sub> to C<sub>8</sub> cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, SO<sub>2</sub>CF<sub>3</sub>, OR<sup>11</sup>, and NR<sup>11</sup>R<sup>12</sup>;

R<sup>8</sup> and R<sup>9</sup> are independent substituents selected from the group consisting of H, C<sub>1</sub> to C<sub>6</sub> alkyl, substituted C<sub>1</sub> to C<sub>6</sub> alkyl, C<sub>3</sub> to C<sub>8</sub> cycloalkyl, substituted C<sub>3</sub> to C<sub>8</sub>

cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, NO<sub>2</sub>, CN, and CO<sub>2</sub>R<sup>10</sup>;

R<sup>10</sup> is selected from the group consisting of C<sub>1</sub> to C<sub>3</sub> alkyl and substituted C<sub>1</sub> to C<sub>3</sub> alkyl;

or CR<sup>8</sup>R<sup>9</sup> comprise a six membered ring having the structure:



R<sup>11</sup> and R<sup>12</sup> are independently selected from the group consisting of H, C<sub>1</sub> to C<sub>6</sub> alkyl, substituted C<sub>1</sub> to C<sub>6</sub> alkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, acyl, substituted acyl, sulfonyl, and substituted sulfonyl;

or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug thereof.

2. The method according to claim 1, further comprising delivering an estrogen in combination with the compound of formula I.

3. The method according to claim 1, wherein the estrogen is delivered prior to or subsequent to the compound of formula I.

4. The method according to claim 1, wherein:

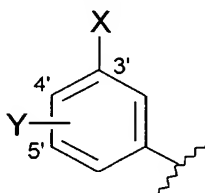
R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of C<sub>1</sub> to C<sub>3</sub> alkyl and substituted C<sub>1</sub> to C<sub>3</sub> alkyl;

or R<sup>1</sup> and R<sup>2</sup> are fused to form the carbon-based 3 to 6 membered saturated spirocyclic ring;

$R^3$  is selected from the group consisting of H, OH,  $NH_2$ ,  $C_1$  to  $C_6$  alkyl, substituted  $C_1$  to  $C_6$  alkyl, and  $COR^C$ ;

$R^C$  is selected from the group consisting of H,  $C_1$  to  $C_4$  alkyl, and  $C_1$  to  $C_4$  alkoxy;

$R^5$  is the substituted benzene ring having the structure:



X is selected from the group consisting of halogen, CN,  $C_1$  to  $C_3$  alkoxy,  $C_1$  to  $C_3$  alkyl,  $NO_2$ ,  $C_1$  to  $C_3$  perfluoroalkyl, 5 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, and  $C_1$  to  $C_3$  thioalkyl.

5. The method according to Claim 1, wherein:

$R^1$  and  $R^2$  are independently selected from the group consisting of  $C_1$  to  $C_3$  alkyl and substituted  $C_1$  to  $C_3$  alkyl;

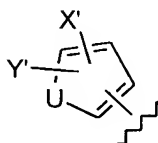
or  $R^1$  and  $R^2$  are fused to form the carbon-based 3 to 6 membered saturated spirocyclic ring;

$R^3$  is selected from the group consisting of H, OH,  $NH_2$ ,  $C_1$  to  $C_6$  alkyl, substituted  $C_1$  to  $C_6$  alkyl, and  $COR^C$ ;

$R^C$  is selected from the group consisting of H,  $C_1$  to  $C_4$  alkyl, and  $C_1$  to  $C_4$  alkoxy;

$R^4$  is selected from the group consisting of H, halogen,  $NO_2$ ,  $C_1$  to  $C_3$  alkyl, and substituted  $C_1$  to  $C_3$  alkyl;

$R^5$  is the five membered ring having the structure:



U is selected from the group consisting of O, S, and  $NR^6$ ;

X' is selected from the group consisting of halogen, CN, C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>3</sub> alkyl, NO<sub>2</sub>, C<sub>1</sub> to C<sub>3</sub> perfluoroalkyl, 5 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, and C<sub>1</sub> to C<sub>3</sub> thioalkyl;

Y' is selected from the group consisting of H, halogen, CN, NO<sub>2</sub>, C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>4</sub> alkyl, and C<sub>1</sub> to C<sub>3</sub> thioalkyl.

6. The method according to claim 1, wherein:

R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of C<sub>1</sub> to C<sub>3</sub> alkyl and substituted C<sub>1</sub> to C<sub>3</sub> alkyl;

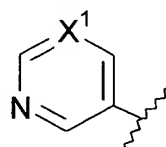
or R<sup>1</sup> and R<sup>2</sup> are fused to form the carbon-based 3 to 6 membered saturated spirocyclic ring;

R<sup>3</sup> is selected from the group consisting of H, OH, NH<sub>2</sub>, C<sub>1</sub> to C<sub>6</sub> alkyl, substituted C<sub>1</sub> to C<sub>6</sub> alkyl, and COR<sup>C</sup>;

R<sup>C</sup> is selected from the group consisting of H, C<sub>1</sub> to C<sub>4</sub> alkyl, and C<sub>1</sub> to C<sub>4</sub> alkoxy;

R<sup>4</sup> is selected from the group consisting of H, halogen, NO<sub>2</sub>, C<sub>1</sub> to C<sub>3</sub> alkyl, and substituted C<sub>1</sub> to C<sub>3</sub> alkyl;

R<sup>5</sup> is the six membered ring having the structure:



X<sup>1</sup> is selected from the group consisting of N and CX<sup>2</sup>;

X<sup>2</sup> is selected from the group consisting of halogen, CN, and NO<sub>2</sub>.

7. The method according to claim 1, wherein R<sup>3</sup> is H and Q<sup>1</sup> is S.

8. The method according to Claim 1, wherein said compound is selected from the group consisting of 6-(3-Chlorophenyl)-4,4-dimethyl-1,4-dihydro-benzo[d][1,3]oxazin-2-thione, 4-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-

benzo[d][1,3]oxazin-6-yl)-thiophene-2-carbonitrile, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl)-5-fluorobenzonitrile, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl)-benzonitrile, 6-(3-fluorophenyl)-4-methyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-4-methylthiophene-2-carbonitrile, tert-Butyl 2-cyano-5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1H-pyrrole-1-carboxylate, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1H-pyrrole-2-carbonitrile, [6-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-pyridin-2-yl]acetonitrile, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile, 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1H-pyrrole-2-carbothiamide, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl) thiophene-3-carbonitrile, 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-ethyl-1H-pyrrole-2-carbonitrile, 4-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazin-4,1-cyclohexan]-6-yl)-2-thiophenecarbonitrile, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-2-fluorobenzonitrile, 6-(5-Bromopyridin-3-yl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Chloro-5-fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Bromo-5-methylphenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Bromo-5-trifluoromethoxyphenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazine-4,1-cyclohexan]-6-yl)-5-fluorobenzonitrile, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-5-methylbenzonitrile, 6-(3,5-Dichlorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 5-(4,4-Dimethyl-1,2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)isophthalonitrile, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-2-furonitrile, 4,4-Diethyl-6-(3-nitrophenyl)-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Chlorophenyl)-4-methyl-4-phenyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 4-Allyl-6-(3-chlorophenyl)-4-methyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-Chloro-5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)benzonitrile, 6-(3,5-Difluorophenyl)-4,4-dimethyl-

1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Fluoro-5-methoxyphenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-5-methoxybenzonitrile, 6-(3-Fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-[3-Fluoro-5-(trifluoromethyl)phenyl]-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(2-Fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3,4-Difluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(4-Fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-4-fluorobenzonitrile, 6-(2,3-Difluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-(8-Bromo-4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-5-fluorobenzonitrile, 4,4-Dimethyl-6-(3-nitrophenyl)-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Chlorophenyl)-4,4-diethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Methoxyphenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(2-Chlorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 4-Benzyl-6-(3-chlorophenyl)-4-methyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Bromo-5-fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl) thiophene-2-carbonitrile, 3-Fluoro-5-(8-fluoro-4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)benzonitrile, 3-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazine-4,1-cyclohexan]-6-yl)benzonitrile, 5-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazine-4,1-cyclohexan]-6-yl)-4-methyl-2-thiophenecarbonitrile, 5-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazine-4,1-cyclohexan]-6-yl)-2-thiophenecarbonitrile, 6-(3-Chloro-4-fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-4-propylthiophene-2-carbonitrile, 4-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-2-furonitrile, 4-Butyl-5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)thiophene-2-carbonitrile, 6-(3-Bromophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, and 2-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-



6-yl)thiophene-3-carbonitrile, or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug thereof.

9. The method according to claim 1, wherein said compound is 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile, or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug thereof.

10. The method according to claim 1, wherein  $R^1$  and  $R^2$  are fused to form a carbon-based 3 to 6 membered saturated spirocyclic ring.

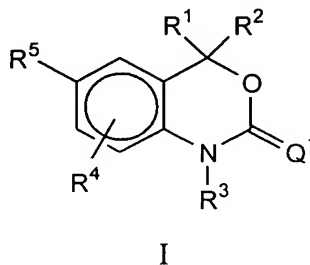
11. The method according to claim 1, wherein  $R^1$  and  $R^2$  are fused to form a carbon-based 3 to 6 membered spirocyclic ring having one or more carbon-carbon double bonds.

12. The method according to claim 1, wherein  $R^1$  and  $R^2$  are fused to form a 3 to 6 membered spirocyclic ring having in its backbone one to three heteroatoms.

13. A composition for conditioning the skin of a mammal:

- (i) a skin conditioning component; and
- (ii) a compound of formula I, or a tautomer thereof, wherein

formula I is:



wherein:

$R^1$  and  $R^2$  are independent substituents selected from the group consisting of H,  $C_1$  to  $C_6$  alkyl, substituted  $C_1$  to  $C_6$  alkyl,  $C_2$  to  $C_6$  alkenyl, substituted  $C_2$  to  $C_6$  alkenyl,  $C_2$  to  $C_6$  alkynyl, substituted  $C_2$  to  $C_6$  alkynyl,  $C_3$  to  $C_8$  cycloalkyl, substituted  $C_3$  to  $C_8$  cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms,  $COR^A$ , and  $NR^B COR^A$ ;

or  $R^1$  and  $R^2$  are fused to form a ring selected from the group consisting of a), b) and c), wherein said ring is optionally substituted by from 1 to 3 substituents selected from the group consisting of H and  $C_1$  to  $C_3$  alkyl;

- a) a carbon-based 3 to 8 membered saturated spirocyclic ring;
- b) a carbon-based 3 to 8 membered spirocyclic ring having one or more carbon-carbon double bonds; and
- c) a 3 to 8 membered spirocyclic ring having in its backbone one to three heteroatoms selected from the group consisting of O, S and N;

$R^A$  is selected from the group consisting of H,  $C_1$  to  $C_3$  alkyl, substituted  $C_1$  to  $C_3$  alkyl, aryl, substituted aryl,  $C_1$  to  $C_3$  alkoxy, substituted  $C_1$  to  $C_3$  alkoxy, amino,  $C_1$  to  $C_3$  aminoalkyl, and substituted  $C_1$  to  $C_3$  aminoalkyl;

$R^B$  is selected from the group consisting of H,  $C_1$  to  $C_3$  alkyl, and substituted  $C_1$  to  $C_3$  alkyl;

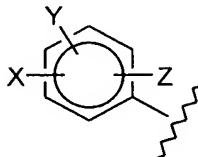
$R^3$  is selected from the group consisting of H, OH,  $NH_2$ ,  $C_1$  to  $C_6$  alkyl, substituted  $C_1$  to  $C_6$  alkyl,  $C_3$  to  $C_6$  alkenyl, substituted  $C_3$  to  $C_6$  alkenyl, alkynyl, substituted alkynyl, and  $COR^C$ ;

$R^C$  is selected from the group consisting of H,  $C_1$  to  $C_4$  alkyl, substituted  $C_1$  to  $C_4$  alkyl, aryl, substituted aryl,  $C_1$  to  $C_4$  alkoxy, substituted  $C_1$  to  $C_4$  alkoxy,  $C_1$  to  $C_4$  aminoalkyl, and substituted  $C_1$  to  $C_4$  aminoalkyl;

$R^4$  is selected from the group consisting of H, halogen, CN,  $NO_2$ ,  $C_1$  to  $C_6$  alkyl, substituted  $C_1$  to  $C_6$  alkyl,  $C_1$  to  $C_6$  alkoxy, substituted  $C_1$  to  $C_6$  alkoxy,  $C_1$  to  $C_6$  aminoalkyl, and substituted  $C_1$  to  $C_6$  aminoalkyl;

$R^5$  is selected from the group consisting of (i) and (ii):

- (i) a substituted benzene ring having the structure:



X is selected from the group consisting of halogen, CN, C<sub>1</sub> to C<sub>3</sub> alkyl, substituted C<sub>1</sub> to C<sub>3</sub> alkyl, C<sub>1</sub> to C<sub>3</sub> alkoxy, substituted C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>3</sub> thioalkyl, substituted C<sub>1</sub> to C<sub>3</sub> thioalkyl, C<sub>1</sub> to C<sub>3</sub> aminoalkyl, substituted C<sub>1</sub> to C<sub>3</sub> aminoalkyl, NO<sub>2</sub>, C<sub>1</sub> to C<sub>3</sub> perfluoroalkyl, substituted C<sub>1</sub> to C<sub>3</sub> perfluoroalkyl, 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR<sup>D</sup>, OCOR<sup>D</sup>, and NR<sup>E</sup>COR<sup>D</sup>;

R<sup>D</sup> is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, substituted C<sub>1</sub> to C<sub>3</sub> alkyl, aryl, substituted aryl, C<sub>1</sub> to C<sub>3</sub> alkoxy, substituted C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>3</sub> aminoalkyl, and substituted C<sub>1</sub> to C<sub>3</sub> aminoalkyl;

R<sup>E</sup> is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, and substituted C<sub>1</sub> to C<sub>3</sub> alkyl;

Y and Z are independent substituents selected from the group consisting of H, halogen, CN, NO<sub>2</sub>, C<sub>1</sub> to C<sub>3</sub> alkoxy, substituted C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>4</sub> alkyl, substituted C<sub>1</sub> to C<sub>4</sub> alkyl, C<sub>1</sub> to C<sub>3</sub> thioalkyl, and substituted C<sub>1</sub> to C<sub>3</sub> thioalkyl;

- b) a five or six membered carbon-based heterocyclic ring having in its backbone 1, 2, or 3 heteroatoms selected from the group consisting of O, S, SO, SO<sub>2</sub> and NR<sup>6</sup> and having one or two independent substituents selected from the group consisting of H, halogen, CN, NO<sub>2</sub>, C<sub>1</sub> to C<sub>4</sub> alkyl, substituted C<sub>1</sub> to C<sub>4</sub> alkyl, C<sub>1</sub> to C<sub>3</sub> alkoxy, substituted C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>3</sub> aminoalkyl, substituted C<sub>1</sub> to C<sub>3</sub> aminoalkyl, C<sub>1</sub> to C<sub>3</sub> perfluoroalkyl, substituted C<sub>1</sub> to C<sub>3</sub> perfluoroalkyl, 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1

to 3 heteroatoms, C<sub>1</sub> to C<sub>3</sub> thioalkyl, substituted C<sub>1</sub> to C<sub>3</sub> thioalkyl, COR<sup>F</sup>, and NR<sup>G</sup>COR<sup>F</sup>;

R<sup>F</sup> is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, substituted C<sub>1</sub> to C<sub>3</sub> alkyl, aryl, substituted aryl, C<sub>1</sub> to C<sub>3</sub> alkoxy, substituted C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>3</sub> aminoalkyl, and substituted C<sub>1</sub> to C<sub>3</sub> aminoalkyl;

R<sup>G</sup> is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, and substituted C<sub>1</sub> to C<sub>3</sub> alkyl;

R<sup>6</sup> is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, and C<sub>1</sub> to C<sub>4</sub> CO<sub>2</sub>alkyl;

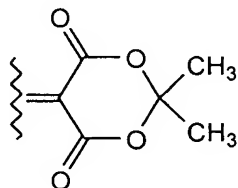
Q<sup>1</sup> is selected from the group consisting of S, NR<sup>7</sup>, and CR<sup>8</sup>R<sup>9</sup>;

R<sup>7</sup> is selected from the group consisting of CN, C<sub>1</sub> to C<sub>6</sub> alkyl, substituted C<sub>1</sub> to C<sub>6</sub> alkyl, C<sub>3</sub> to C<sub>8</sub> cycloalkyl, substituted C<sub>3</sub> to C<sub>8</sub> cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, SO<sub>2</sub>CF<sub>3</sub>, OR<sup>11</sup>, and NR<sup>11</sup>R<sup>12</sup>;

R<sup>8</sup> and R<sup>9</sup> are independent substituents selected from the group consisting of H, C<sub>1</sub> to C<sub>6</sub> alkyl, substituted C<sub>1</sub> to C<sub>6</sub> alkyl, C<sub>3</sub> to C<sub>8</sub> cycloalkyl, substituted C<sub>3</sub> to C<sub>8</sub> cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, NO<sub>2</sub>, CN, and CO<sub>2</sub>R<sup>10</sup>;

R<sup>10</sup> is selected from the group consisting of C<sub>1</sub> to C<sub>3</sub> alkyl and substituted C<sub>1</sub> to C<sub>3</sub> alkyl;

or CR<sup>8</sup>R<sup>9</sup> comprise a six membered ring having the structure:



R<sup>11</sup> and R<sup>12</sup> are independently selected from the group consisting of H, C<sub>1</sub> to C<sub>6</sub> alkyl, substituted C<sub>1</sub> to C<sub>6</sub> alkyl, aryl, substituted aryl, carbon-based heterocyclic

ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, acyl, substituted acyl, sulfonyl, and substituted sulfonyl;

or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug thereof.

14. The composition according to Claim 13, wherein said compound is selected from the group consisting of 6-(3-Chlorophenyl)-4,4-dimethyl-1,4-dihydrobenzo[d][1,3]oxazin-2-thione, 4-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl)-thiophene-2-carbonitrile, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl)-5-fluorobenzonitrile, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl)-benzonitrile, 6-(3-fluorophenyl)-4-methyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-4-methylthiophene-2-carbonitrile, tert-Butyl 2-cyano-5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1H-pyrrole-1-carboxylate, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1H-pyrrole-2-carbonitrile, [6-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-pyridin-2-yl]acetonitrile, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile, 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1H-pyrrole-2-carbothiamide, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl) thiophene-3-carbonitrile, 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-ethyl-1H-pyrrole-2-carbonitrile, 4-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazin-4,1-cyclohexan]-6-yl)-2-thiophenecarbonitrile, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-2-fluorobenzonitrile, 6-(5-Bromopyridin-3-yl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Chloro-5-fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Bromo-5-methylphenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Bromo-5-trifluoromethoxyphenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazine-4,1-cyclohexan]-6-yl)-5-fluorobenzonitrile, 3-(4,4-Dimethyl-2-thioxo-

1,4-dihydro-2H-3,1-benzoxazin-6-yl)-5-methylbenzonitrile, 6-(3,5-Dichlorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 5-(4,4-Dimethyl-1,2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)isophthalonitrile, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-2-furonitrile, 4,4-Diethyl-6-(3-nitrophenyl)-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Chlorophenyl)-4-methyl-4-phenyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 4-Allyl-6-(3-chlorophenyl)-4-methyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-Chloro-5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)benzonitrile, 6-(3,5-Difluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Fluoro-5-methoxyphenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-5-methoxybenzonitrile, 6-(3-Fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-[3-Fluoro-5-(trifluoromethyl)phenyl]-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(2-Fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3,4-Difluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(4-Fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-4-fluorobenzonitrile, 6-(2,3-Difluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-(8-Bromo-4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-5-fluorobenzonitrile, 4,4-Dimethyl-6-(3-nitrophenyl)-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Chlorophenyl)-4,4-diethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Methoxyphenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(2-Chlorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 4-Benzyl-6-(3-chlorophenyl)-4-methyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Bromo-5-fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl) thiophene-2-carbonitrile, 3-Fluoro-5-(8-fluoro-4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)benzonitrile, 3-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazine-4,1-cyclohexan]-6-yl)benzonitrile, 5-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazine-4,1-cyclohexan]-6-

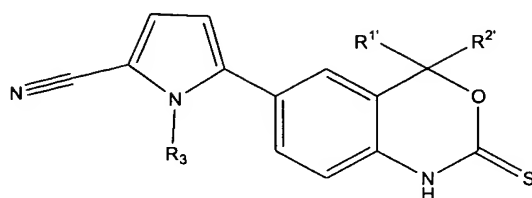
yl)-4-methyl-2-thiophenecarbonitrile, 5-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazine-4,1-cyclohexan]-6-yl)-2-thiophenecarbonitrile, 6-(3-Chloro-4-fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-4-propylthiophene-2-carbonitrile, 4-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-2-furonitrile, 4-Butyl-5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)thiophene-2-carbonitrile, 6-(3-Bromophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, and 2-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)thiophene-3-carbonitrile, or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug thereof.

15. The composition according to claim 13, where the compound is 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile, or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug thereof.

16. The composition according to claim 13, wherein in the compound of formula I,  $R^3$  is H and  $Q^1$  is S.

17. A method of conditioning the skin comprising the step of delivering to a subject the composition of claim 14.

18. A progesterone receptor modulator of formula II, wherein formula II has the structure:



II

wherein:

R<sup>1'</sup> is selected from the group methyl, ethyl, trifluoromethyl;

R<sup>2'</sup> is selected from the group methyl, ethyl, trifluoromethyl;

or

R<sup>1'</sup> and R<sup>2'</sup> are joined to form a spirocyclic ring containing 3 to 7 carbon atoms; and R<sup>3'</sup> is selected from the group C<sub>1</sub> to C<sub>4</sub> alkyl, and tautomers, prodrugs, metabolites, or pharmaceutically acceptable salts thereof.

19. A progesterone receptor modulator according to claim 18, wherein said compound is selected from the group consisting of 5-(4-ethyl-4-methyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile, 5-(4,4-diethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile, 1-methyl-5-(2-thioxo-1,2-dihydrospiro[3,1-benzoxazine-4,1'-cyclobutan]-6-yl)-1H-pyrrole-2-carbonitrile, 1-methyl-5-(2-thioxo-1,2-dihydrospiro[3,1-benzoxazine-4,1'-cyclohexan]-6-yl)-1H-pyrrole-2-carbonitrile, 1-methyl-5-(2-thioxo-1,2-dihydrospiro[3,1-benzoxazine-4,1'-cyclopentan]-6-yl)-1H-pyrrole-2-carbonitrile, 1-methyl-5-[2-thioxo-4,4-bis(trifluoromethyl)-1,4-dihydro-2H-3,1-benzoxazine-6-yl]-1H-pyrrole-2-carbonitrile, prodrugs, metabolites, or pharmaceutically acceptable salts thereof..



20. A pharmaceutical composition comprising a progesterone receptor modulator of Claim 18 and a pharmaceutically acceptable carrier or excipient.

21. A method of inducing contraception in a mammal, the method comprising administering to a mammal in need thereof a pharmaceutically effective amount of a progesterone receptor modulator of Claim 18.

22. A method of treating hormone-dependent neoplastic disease in a mammal, the method comprising administering to a mammal in need thereof a pharmaceutically effective amount of a progesterone receptor modulator of Claim 18.

23. The method of Claim 22 wherein the hormone-dependent neoplastic disease is selected from the group of uterine myometrial fibroids, endometriosis, benign prostatic hypertrophy; carcinomas and adenocarcinomas of the endometrium, ovary, breast, colon, prostate, pituitary, and meningioma.

24. A method of synchronizing estrus in a mammal, the method comprising administering to a mammal in need thereof a pharmaceutically effective amount of a progesterone receptor modulator of Claim 18 or a pharmaceutically acceptable salt thereof.

25. A method of administering hormone replacement therapy, the method comprising administering to a mammal in need thereof a pharmaceutically effective amount of a progesterone receptor modulator of Claim 18 or a pharmaceutically acceptable salt thereof.

26. A method of treating a skin disorder, the method comprising administering to a mammal in need thereof a pharmaceutically effective amount of a progesterone receptor modulator of Claim 18 or a pharmaceutically acceptable salt thereof.

27. The method according to claim 26, wherein the skin disorder is selected from the group consisting of acne and hirsutism.